

REMARKS

Entry of the foregoing, and early and favorable consideration of the subject application are respectfully requested. By the present amendment, claims 127-132 and 134-143 have been canceled without prejudice to or disclaimer of the subject matter contained therein. Claim 133 has been amended to recite a method for detecting a chromosomal deletion employing two distinguishably labeled probe sets. New claim 144 has been added; this claim depends from claim 133, but adds the further limitation that unlabeled blocking DNA is hybridized to the chromosome. This new claim derives support at least from page 67, lines 5-19 of the specification as originally filed. No new matter has been added.

Interview Summary

Applicants gratefully acknowledge the courtesy shown to their undersigned representative by the Examiner in the personal interview held on September 22, 2010. At that interview, Applicants' representative offered to amend the claims as shown herein. The Examiner indicated that such an amendment would overcome the rejections of the claims under 35 USC §112, ¶1 (written description and enablement).

Priority

At pages 2-3 of the Official Action, the Examiner notes several apparent errors in the priority claim as amended in Applicants' response filed July 8, 2010. By the present Amendment, the priority claim has been amended to correct these minor and typographical errors.

Information Disclosure Statement

Applicants acknowledge the indication by the Examiner, at page 5 of the Official Action, that some of the publications submitted with the 25 May 2010 IDS were not legible. Applicants will resubmit the missing references.

Oath/Declaration

Applicants acknowledge the indication by the Examiner, at page 5 of the Official Action, that the "Declaration filed 30 June 2003 does not identify the instant application or the preliminary amendment that contains subject matter not present in the application number identified on the declaration." Applicants note that the Declaration originally submitted with the instant application is the declaration that was first submitted in connection with application Serial No. 07/537,305, which includes the same specification as the present application. Amended claim 133, and new claim 143, recite a method for detecting a chromosomal deletion; this subject matter was disclosed and claimed in the originally-filed application (*see, e.g.*, p. 3, lines 12-15; p. 13, line 14 - page 14, line 2; page 19, lines 3-18; page 25, line 18 - page 26, line 2; page 103, lines 4-15; page 115, lines 1-4; Figure 11 F; and original claims 7, 22, and 32). Accordingly, Applicants respectfully submit that a substitute declaration is not required in the present application.

Drawings

Applicants acknowledge the objection to the drawings by the Examiner, at page 6 of the Official Action. Applicants agree to submit color copies of the

drawings in the instant application, and the appropriate petition, upon indication that the claims are otherwise allowable.

Claim Rejections - 35 USC 112

Claims 133, 134, and 141-143 stand rejected under 35 USC 112, first paragraph, as purportedly not supported by an adequate written description in the specification. This rejection, to the extent that it applies to the claims as amended, is respectfully traversed.

Applicants respectfully disagree with the Examiner's arguments, set forth at pages 6-8 of the Official Action, regarding the support for the full scope of the claims in this application. In particular, at page 6, the Examiner argues that the specification suggests that the probes that hybridize to a deletion region should not be used, quoting the following passage from pp. 32-33 of the specification: "A deletion could also be detected with a probe that stains only deleted regions; however, lack of probe binding may be due to reasons other than deletion of the target sequence." Applicants respectfully submit that, read in context, this passage is not properly interpreted to teach away from using probes that hybridize to a deletion region. The full passage from pp. 32-33, which describes Figure 11f, reads as follows:

Section f) represents a staining pattern useful in the detection of a deletion. A deletion could also be detected with a probe that stains only the deleted region; however, lack of probe binding may be due to reasons other than deletion of the target sequence. The flanking regions stained a different "color" serve as controls for hybridization.

Applicants submit that this passage cautions against attempts to detect deletions using a single probe, because a lack of probe binding may be due to reasons other than a deletion, such as problems with experimental technique or reagents. Use of

a second, differentially labeled probe set, which labels the regions flanking the deletion region, as taught herein and presently claimed, overcomes this problem by providing a positive control. If the probe to the deletion region does not bind, but the probe to the flanking region does, it may be safely concluded that the deletion is present. If neither probe set binds, then there is a problem with the hybridization conditions more generally, that will need to be overcome before any conclusion can be drawn about the presence of a deletion.

Claims 133, 134, and 141-143 stand rejected under 35 USC 112, second paragraph, as purportedly indefinite in the use of the phrase "sufficient in length and substantially complementary to a deletion region of a chromosome," and the phrase "said first probe set will hybridize to the deletion region." This rejection, to the extent that it applies to the claims as amended, is respectfully traversed.

At page 8 of the Official Action, the Examiner argues that "a probe cannot be complementary to a region that is absent from a chromosome." The Examiner suggests that amending the claims to recite "a probe set sufficient in length and substantially complementary to a region that has been deleted from a chromosome" would overcome the rejection. Applicants respectfully submit that the suggested phrase would not solve the purported problem, as it would require the probe to hybridize to DNA that has been deleted and, thus, is not present. Applicants note that the claim refers to a "deletion region," not a "*deleted* region." In the context of the present specification, a deletion region is a region in which a diagnostically or prognostically important deletion *may* occur. See, e.g., p. 25, lines 23-25. Applicants maintain that one of ordinary skill in the art would understand that the aim of the claims is to detect the presence or absence of the deletion region, not to

hybridize to DNA that is not present. Accordingly, withdrawal of this rejection is believed to be in order, and is respectfully requested.

Claim Rejections - 35 USC 103

Claims 133, 134, and 141-143 stand rejected under 35 USC 103(a) as purportedly obvious over Dryja et al. (*PNAS* 83:7391-7394 (1986)). This rejection, to the extent that it applies to the claims as amended, is respectfully traversed.

At page 11 of the Official Action, the Examiner concedes that "Dryja et al. does not show a product comprising the two labeled chromosomal probes, ... One of which [comprising] a probe that hybridizes to a region flanking the region that has been deleted." Applicants respectfully submit that there is no disclosure in Dryja, and the Examiner has pointed to none, that would lead one of ordinary skill in the art at the time the presently claimed invention was made, to have modified the method disclosed by Dryja to incorporate two probe sets, differentially labeled, as required by the instant claims. Accordingly, the present claims are not *prima facie* obvious over Dryja et al., and withdrawal of this rejection is respectfully requested.

CONCLUSION

From the foregoing, further and favorable action in the form of a Notice of Allowance is believed to be next in order, and such action is earnestly solicited.

In the event that there are any questions concerning this paper, or the application in general, the Examiner is respectfully urged to telephone Applicants undersigned representative so that prosecution of the application may be expedited.

The Commissioner is hereby authorized to charge any fees required by this paper, and to credit any overpayment, to Deposit Account No. 50-4047 (Order No. 7045945002).

Respectfully submitted,

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